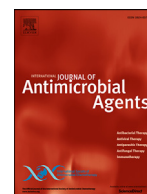




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Letter to the Editor

Effect of hydroxychloroquine and azithromycin on the viral clearance of SARS-CoV-2: response to Hervé Seligmann


Dear Editor,

We read Hervé Seligmann's balanced comments regarding our work with great interest [1]. He raises the possibility of false negative PCR results that may have possibly influenced our results. However, it is worthy to note that the negative results at end of our follow-up were preceded by two or more negative tests in 93% of the treated patients, and that we used an internal control of PCR. Regarding missing PCR data, the results were considered positive if the PCR results performed the day before and the day after were both positive. In contrast, they were considered negative if the results of at least one of the two previous consecutive days were negative (according to the European Centre for Disease Prevention and Control, the patients can be discharged from hospital if at least two consecutive RT-PCR tests are negative in respiratory samples (<https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-guidance-discharge-and-ending-isolation-firstupdate.pdf>)).

Hervé Seligmann's statistical approach in analysing our data on the effect of hydroxychloroquine and azithromycin on the viral clearance in COVID-19 patients [2] is pertinent and shows evidence of a cumulative, systematic and gradual effect of the treatment on reducing SARS-CoV-2 carriage. Following suggestions from other colleagues we reanalysed our data without patient exclusion and using some statistical methods better adapted to small series, including Barnard and Wang tests; estimates of effect modification such as relative risk reduction, absolute risk reduction and number needed to treat; mixed effect logistic regression model; and logistic and linear regression models [3–6]. These different approaches confirmed our results. Toumi and Aballea reanalyzed our results using the last-observation-carried-forward imputation conservative method and also confirmed our results [7]. Finally, a meta-analysis of available studies evaluating the effect of hydroxychloroquine on SARS-CoV-2 clearance confirmed the significant effect of this drug [8].

In conclusion, despite the many passionate and sometimes acerbic criticisms that our imperfect study has raised, it clearly seems that our results are robust and confirm the need for large-scale

studies on the effect of hydroxychloroquine and azithromycin on both SARS-CoV-2 clearance and clinical benefit in COVID-19 patients.

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